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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,673	05/08/2001	Jonathan M.J. Derry	3198	3258

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EXAMINER
SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
1631	16

DATE MAILED: 08/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,673	DERRY ET AL.	
	Examin r	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspond nc address --

Period f r R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-39* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *12* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendments and remarks in Paper No. 15, filed 5/19/03, are acknowledged. Canceled claim 2 and new claims 25-39 are acknowledged.

Applicant's arguments, filed 5/19/03, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The IDS, filed 2/3/03, has been considered.

Claims 25-39 are herein under examination.

The arguments for claim 2 are rendered moot as this claim has been cancelled.

Claim Objections

Claim 26 is objected to because of the following informalities: It is not in proper Markush form, because the word "and" is missing on line 4 of the claim. Appropriate correction is required. This objection is necessitated by amendment.

Claims Rejected Under 35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF SCOPE OF ENABLEMENT

Claims 25-39 are rejected under 35 U.S.C. §112, first paragraph. While being enabling (subject to the lack of enablement rejection) for identifying compounds that inhibit the binding activity between full-length polypeptides of NEMO and CYLD, the specification does not reasonably provide enablement for identifying compounds that inhibit the binding activity of NEMO and CYLD polypeptides via fragments and variants. The claim is broader than the enablement provided by the disclosure with regard to the large number of possible fragments and variants that could be utilized which may or may not still exhibit NEMO and CYLD characteristics. The specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the instant claim. This rejection is necessitated by amendment.

LACK OF ENABLEMENT

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology

is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Claims 25-39 are directed to a method for identifying compounds that inhibit the binding activity between NEMO and CYLD polypeptides, fragments, and variants. However, claims 25-39 do not adequately limit the fragments and variants of NEMO and CYLD that still contain the NEMO and CYLD characteristics and properties including their binding activities.

It would require undue experimentation for a person having ordinary skill in the art to practice the claimed invention due to the unpredictability of knowing what degree of variance or what fragment involved would still allow the NEMO and CYLD polypeptides to be biologically active. The NEMO and CYLD components used directly affect the outcome of the claimed method, and Applicants have not shown how independent variation of one or more components in the scheme would affect the outcome of the claimed method. Due to the above-mentioned unpredictability, a skilled artisan would not be able to practice the claimed invention without undue experimentation.

Applicants state that the fragments and variants of the claimed invention are at least 80% identical to the polypeptides set forth in the sequence listing and retain the ability to bind the respective binding partner (Response filed 5/19/03, on page 14 (last paragraph) to 15 (first paragraph)). This is found unpersuasive as the fragments on lines 10 and 17 of instant claim 25 and on lines 8 and 15 of instant claim 34 are not limited to the 80% identity as stated by Applicants. Applicants submit that it is a matter of routine experimentation to make such fragments and variants, evaluate whether they are at least 80% identical to the native polypeptides, and determine if they are capable of binding the other binding partner (Response,

page 15, first paragraph). This is found unpersuasive due to the unpredictability of knowing for each fragment and variant claimed that they still feature the biological activity of NEMO and CYLD polypeptides. A fragment or variant that is 80% similar to the native polypeptide does not guarantee the fragment or variant is still biologically active. It is noted that even a single amino acid or nucleotide change in a sequence can result in significant changes to a particular polypeptide or nucleic acid (see sequence comparison discussion in previous Office action on pages 5-6, mailed 1/15/03).

This rejection is necessitated by amendment.

LACK OF WRITTEN DESCRIPTION

Claims 25-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification discloses SEQ ID NOs: 2 and 4 which correspond to NEMO and CYLD polypeptides, respectively. SEQ ID NOs: 2 and 4 meet the written description provisions of 35 USC 112, first paragraph. However, claims 25 and 34 are directed to encompass "fragments" and "variants ... that are at least 80% identical" to SEQ ID NO: 2 and 4. The only fragments or variants that meet the written description provision of 35 USC 112, first paragraph, are fragment 287-419 of SEQ ID NO: 2 and the fragments listed on page 9 (line 30) to page 10 (line 9). However, due to the open claim language of "comprising" in claims 25 (lines 6, 8, and 15), 26 (lines 3 and 5), and 27 (lines 3 and 4) as well as "consisting essentially of" in claims 34 (lines 4, 6, and 13) and 35 (lines 3 and 5), these claims encompass other polypeptide sequences that do not meet the written description provision of 35 USC 112, first paragraph. The

specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 2 and 4, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NOs: 2 and 4, fragment 287-419 of SEQ ID NO: 2, and the fragments listed on pages 9-10 of the specification, but not the full breadth of the claim meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded

that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) This rejection is necessitated by amendment.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25 and 34 are vague and indefinite due to the unclarity of citing an abbreviation, such as "NF-kappaB" (claim 25, line 2) and "CD40" (claim 25 (line 24) and claim 34 (line 22)). Correction is suggested by amending in of the full name in parentheses. Claims 26-33 and 35-39 are also rejected due to their direct or indirect dependency from claims 25 and 34. This rejection is necessitated by amendment.

Claims 25 (line 23) and 34 (line 21-22) recite the phrase "inhibition of binding... by at least 50%" which is vague and indefinite. It is unclear to what the 50% is referring. For example, the "at least 50%" may be referring to 50% of the surface of the molecules being bound, to 50% of trial cases testing inhibition, or countless other scenarios. Clarification of the metes and bounds of the instant claim with clearer claim wording is required. Claims 26-33 and 35-39 are also rejected due to their direct or indirect dependency from claims 25 and 34. This rejection is necessitated by amendment.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 4, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER